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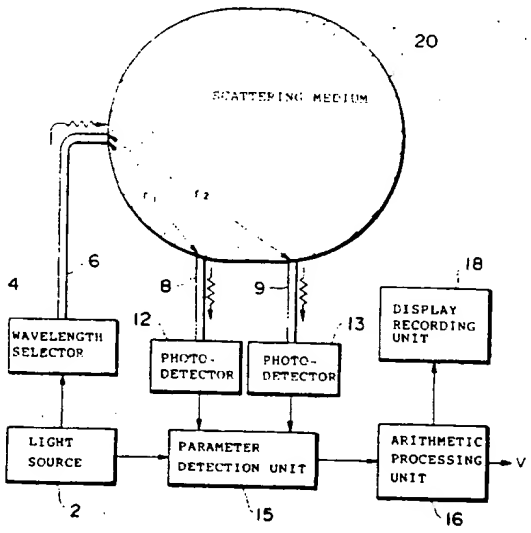
(54) Method and apparatus for measuring concentration of absorptive constituent in scattering medium

(57) A method for measuring a concentration of an absorptive constituent in a scattering medium comprises the steps of emitting two or more kinds of light having predetermined wavelengths; making said light incident at a light incidence position into said scattering medium, detecting said light at one or more photodetection points to acquire one or more photodetection signals detecting light quantities and average flight pathlengths for said respective kinds of light based on said signals and obtaining a concentration of said absorptive constituent by arithmetic processing using said light quantities and average flight pathlengths based on a predetermined relationship. The method permits absolute-value measurement of the concentration of the absorptive constituent inside the scattering medium having various exterior shapes.

Fig. 4



STRUCTURE OF APPARATUS OF THE FIRST EMBODIMENT

EP 0 703 445 A2

Description

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a method and apparatus for measuring the absolute concentration of absorptive constituent in a scattering medium. which is so arranged that two or more kinds of light having predetermined wavelengths. at which the scattering coefficients are equal or regarded as equal. are made incident into the scattering medium such as a living tissue. which could take a variety of exterior shapes. and that the light of the predetermined wavelengths is detected after diffusively having propagated through inside the scattering medium and when escaping from the surface thereof. to obtain quantities of light and average flight pathlengths (average optical pathlengths) at one or more positions of detection. whereby the concentration of a specific absorptive constituent inside the scattering medium or the absolute amount thereof. an oxygen saturation of hemoglobin. and further. a time change or spatial distribution thereof can be measured at high accuracy and in a non-invasive fashion without being affected by the exterior shape of the scattering medium.

Related Background Art

There are very high demands for non-invasive and precise measurement of the concentration of a specific absorptive constituent inside the scattering medium such as a living tissue or the absolute amount thereof. and a time change or spatial distribution thereof in addition. and a variety of methods and attempts have been made to meet the demands. for example methods using continuous light (CW light) or modulated light (for example. pulsed light. square-wave light. sinusoidally modulated light. etc). methods utilizing light beams with different wavelengths. etc

These conventional techniques. however. do not have developed a satisfactory method or apparatus for accurately measuring the concentration of a specific absorptive constituent in various media which could take a variety of shapes. such as a living tissue. or a particular tissue which usually has individual differences in shape This has been a serious problem in non-invasive measurement of living samples utilizing the light. and improvement has strongly been desired therein.

The light incident into the scattering medium such as a living tissue diffusively propagates inside the medium while scattered and absorbed. and then part thereof comes out of the surface of the medium Since the outside of the scattering medium is normally filled with air. the light escaping from the surface dispersively propagates in a free space

For measuring information on the inside of the scattering medium. the light escaping from the surface is detected as described above With scattering media in different shapes. for example depending upon sphere or rectangular parallelepiped. a great difference will appear in quantity or behavior of the light escaping from a predetermined position of the surface therefrom.

Therefore. in order to improve the accuracy of such measurement. it is necessary to understand the behavior of the light inside the scattering medium. It is recently known that the behavior of the light inside the scattering medium can be analyzed. experimented. or investigated by the Monte Carlo calculation (Monte Carlo simulation) using a computer. or can be described or analyzed accurately to some extent by the photon diffusion theory.

As described above. the Monte Carlo simulation and photon diffusion theory have been used heretofore in order to understand the behavior of the light inside the scattering medium.

SUMMARY OF THE INVENTION

The inventor found out that the above conventional methods included the following problems.

Namely. the Monte Carlo simulation requires a very long time for calculation and does not permit us to calculate the concentration etc. of the specific absorptive constituent inside the scattering medium from the result.

In utilizing the photon diffusion theory. it is necessary to set boundary conditions in order to actually solve photon diffusion equations. However. the boundary conditions are greatly dependent on the exterior shape of scattering medium: thus. for accurate measurement. new boundary conditions must be set for each of scattering media with different shapes to solve photon diffusion equations therefor. Further. shapes of scattering media for which the boundary conditions can be set accurately to some extent are limited to extremely simple ones. such as an infinite space. a semi-infinite space. an infinite circular cylinder. an infinitely spreading slab with a finite thickness. and so on. Consequently. approximate boundary conditions have to be used for measurement of an object of a complex shape. such as a living tissue. which causes a great measurement error.

As described above. the conventional technology has failed to develop a method for handling diffusing light. which was capable of being systematically applied to scattering media of different shapes. and therefore. it is impossible to

accurately measure concentrations etc. of a specific absorptive constituent inside the scattering media having different shapes by systematically applying the conventional techniques.

Solving the above problems, an object of the present invention is to provide a method and apparatus for measuring a concentration of an absorptive constituent inside a scattering medium, which newly discloses basic relationships associated with the behavior of the light inside the scattering media of different shapes, which realizes measurement of concentrations or absolute amounts of a specific absorptive constituent inside the scattering media having various shapes, etc., utilizing the relationships, which greatly improves the accuracy of the measurement, and which can measure a time change or spatial distribution of those.

The present invention involves such a technique that two or more kinds of light having predetermined wavelengths, at which the scattering coefficients are equal or regarded as equal, are made incident into a scattering medium, which could take various exterior shapes, light quantities and average flight pathlengths are obtained at a position of photodetection for the light of the predetermined wavelengths, and from these values, a concentration or an absolute amount of a specific absorptive constituent is obtained by arithmetic processing without being affected by the shape of scattering medium.

The present invention provides a method for measuring a concentration of an absorptive constituent in a scattering medium, comprising:

(a) a step of emitting two or more kinds of light having predetermined wavelengths (light having two or more predetermined wavelengths), at which the scattering coefficients are equal or regarded as equal, toward a scattering medium which is a measured object.

(b) a step of making the light incident into the scattering medium at a light incidence position and making the light propagate through the scattering medium.

(c) a step of detecting the light having propagated through the scattering medium, at one or more photodetection points different from the light incidence position to obtain one or more photodetection signals.

(d) a step of detecting light quantities and average flight pathlengths at the one or more photodetection points for the respective kinds of light having the wavelengths, based on the one or more photodetection signals, and

(e) a step of obtaining a concentration of the absorptive constituent by arithmetic processing using the light quantities and the average flight pathlengths, based on a predetermined relationship as to the light quantities, the average flight pathlengths, and a difference between absorption coefficients per unit concentration of the absorptive constituent for the respective kinds of light having the wavelengths.

The two or more kinds of light having predetermined wavelengths may be two or more kinds of pulsed light having predetermined wavelengths.

The two or more kinds of light having predetermined wavelengths may be two or more kinds of sinusoidally modulated light having a predetermined modulation frequency component, the light quantities may be calculated from (i) dc components of the photodetection signals or (ii) amplitudes of the predetermined modulation frequency component (signal) included in the photodetection signals, and the average flight pathlengths may be calculated from phase delays (phase differences) of the predetermined modulation frequency component (signal) included in the photodetection signals

Further, the two or more kinds of light having predetermined wavelengths may be two or more kinds of modulated light having a predetermined repetitive modulation frequency component, the light quantities may be calculated from (i) dc components of the photodetection signals or (ii) amplitudes of the predetermined repetitive modulation frequency component (signal) or a frequency component (signal) of an integral multiple thereof, included in the photodetection signals, and the average flight pathlengths may be calculated from phase delays (phase differences) of the predetermined repetitive modulation frequency component (signal) or a frequency component (signal) of an integral multiple thereof, included in the photodetection signals.

The predetermined relationship among the light quantities, the average flight pathlengths, and the difference between the absorption coefficients per unit concentration of the absorptive constituent for the respective kinds of light having the wavelengths is preferably a relationship derived from such a relation that a partial differentiation of a natural logarithm of a light quantity detected with respect to an absorption coefficient is equal to an average flight pathlength.

In one embodiment of the method of the present invention, the above step (e) comprises obtaining the concentration of the absorptive constituent in the scattering medium by arithmetic processing using the light quantities and the average flight pathlengths, based on the relationship expressed by the following formula:

$$V = (\epsilon_2 - \epsilon_1)^{-1} \times [p\langle L_1(\lambda_1)\rangle + (1 - p)\langle L_1(\lambda_2)\rangle]^{-1} \times \ln[I_1(\lambda_1)/I_1(\lambda_2)]$$

where

V: the concentration of the absorptive constituent.

ϵ_1: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1.

ϵ_2: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2

$\langle L_1(\lambda_1)\rangle$: the average flight pathlength of the incident light of the wavelength λ_1 at a photodetection point r_1

$\langle L_1(\lambda_2)\rangle$: the average flight pathlength of the incident light of the wavelength λ_2 at the photodetection point r_1.

$I_1(\lambda_1)$: the (normalized) quantity of detected light for the incident light of the wavelength λ_1 at the photodetection point r_1.

$I_1(\lambda_2)$: the (normalized) quantity of detected light for the incident light of the wavelength λ_2 at the photodetection point r_1, and

p: a predetermined value, to satisfy the condition of $0 \leq p \leq 1$.

In another embodiment of the method of the present invention, the above step (e) comprises obtaining the concentration of the absorptive constituent in the scattering medium by arithmetic processing using the light quantities and the average flight pathlengths, based on a relationship expressed by the following formula:

$$V = (\epsilon_2 - \epsilon_1)^{-1} \times [p\langle L_1(\lambda_1)\rangle + (1 - p)\langle L_1(\lambda_2)\rangle - q\langle L_2(\lambda_1)\rangle - (1 - q)\langle L_2(\lambda_2)\rangle]^{-1} \times \ln\{[I_1(\lambda_1)\cdot I_2(\lambda_2)]/[I_1(\lambda_2)\cdot I_2(\lambda_1)]\}$$

where

V: the concentration of the absorptive constituent.

ϵ_1: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1

ϵ_2: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2

$\langle L_1(\lambda_1)\rangle$: the average flight pathlength at a photodetection point r_1, of the incident light of the wavelength λ_1

$\langle L_1(\lambda_2)\rangle$: the average flight pathlength at the photodetection point r_1, of the incident light of the wavelength λ_2.

$\langle L_2(\lambda_1)\rangle$: the average flight pathlength at a photodetection point r_2, of the incident light of the wavelength λ_1.

$\langle L_2(\lambda_2)\rangle$: the average flight pathlength at the photodetection point r_2, of the incident light of the wavelength λ_2.

$I_1(\lambda_1)$: the quantity of detected light at the photodetection point r_1, for the incident light of the intensity B_1 and the wavelength λ_1.

$I_1(\lambda_2)$: the quantity of detected light at the photodetection point r_1, for the incident light of the intensity B_2 and the wavelength λ_2.

$I_2(\lambda_1)$: the quantity of detected light at the photodetection point r_2, for the incident light of the intensity B_1 and the wavelength λ_1.

$I_2(\lambda_2)$: the quantity of detected light at the photodetection point r_2, for the incident light of the intensity B_2 and the wavelength λ_2.

p: a predetermined value to satisfy the condition of $0 \leq p \leq 1$, and

q: a predetermined value to satisfy the condition of $0 \leq q \leq 1$.

The present invention also provides an apparatus for measuring a concentration of an absorptive constituent in a scattering medium, comprising:

(a) a light source for emitting two or more kinds of light having predetermined wavelengths, at which the scattering coefficients are equal or regarded as equal, toward a scattering medium which is a measured object;

(b) light incidence means for making the light incident at a light incidence position into the scattering medium and then making the light propagate through the scattering medium;

(c) light detecting means (photodetection means) for detecting the light having propagated through the scattering

medium. at one or more photodetection points different from the light incidence position to obtain one or more photodetection signals.

(d) parameter detecting means for detecting light quantities and average flight pathlengths at the one or more photodetection points for the respective kinds of light having the wavelengths. based on the one or more photodetection signals· and

(e) arithmetic processing means for obtaining a concentration of the absorptive constituent by arithmetic processing using the light quantities and the average flight pathlengths. based on a predetermined relationship among the light quantities. the average flight pathlengths. and a difference between absorption coefficients per unit concentration of the absorptive constituent for the respective kinds of light having the wavelengths.

Here. the arithmetic processing means (e) is preferably arranged to obtain the concentration of the absorptive constituent. based on the predetermined relationship among the light quantities. the average flight pathlengths. and the difference between the absorption coefficients per unit concentration of the absorptive constituent for the respective kinds of light having the wavelengths. which is derived from such a relation that a partial differential of a natural logarithm of the quantity of detected light with respect to the absorption coefficient is equal to the average flight pathlength.

Since the present invention involves arithmetic processing of the concentration of the specific absorptive constituent. based on the basic relationship holding for various scattering media of different shapes. that is. based on the relationship among the light quantities and the average flight pathlengths at a detection point. and the difference between absorption coefficients per unit concentration of the absorptive constituent for the two or more kinds of light having predetermined wavelengths. the concentration of the specific absorptive constituent can be accurately measured without being affected by the exterior shape of scattering medium. Also. the invention permits us to measure a time change or spatial distribution of the concentration of the specific absorptive constituent

The present invention uses the light quantities and average flight pathlengths obtained from actually measured values. as parameters for the arithmetic processing of the concentration of the specific absorptive constituent Since these parameters are those obtainable by utilizing almost all light gathered at the photodetection point. that is. those obtained in the integral form. high signal-to-noise ratios can be achieved. thereby achieving high measurement accuracy as a result.

In the present invention. the two or more kinds of light having predetermined wavelengths. at which the scattering coefficients are equal or regarded as equal are let to be incident into the scattering medium. measurement is carried out for the light. the difference between the absorption coefficients of the absorptive constituent at the predetermined wavelengths is calculated from measured values. and the concentration of the specific absorptive constituent is obtained therefrom. On this occasion if light signals are detected at two or more detection points. a difference between light quantities of incident light beams of different wavelengths can be eliminated. which permits more practical measurement with high accuracy

The present invention will become more fully understood from the detailed description given hereinbelow and the accompanying drawings which are given by way of illustration only. and thus are not to be considered as limiting the present invention.

Further scope of applicability of the present invention will become apparent from the detailed description given hereinafter. However. it should be understood that the detailed description and specific examples. while indicating preferred embodiments of the invention. are given by way of illustration only. since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is an explanatory drawing of a track of light having propagated through the inside of a scattering medium:

Fig. 2 is an explanatory drawing to show an example of time-resolved re-emission measured:

Fig. 3 is a graph to show absorption spectra of various biological materials:

Fig. 4 is a structural drawing of an apparatus of the first embodiment:

Fig. 5 to Fig. 8 are each explanatory drawings to show respective methods for guiding light into a scattering medium:

Fig. 9 to Fig. 11 are each explanatory drawings to show respective methods for receiving light:

Fig. 12 is a structural drawing of an apparatus of the second embodiment:

Fig. 13 is a structural drawing of light incidence and photodetection portions the apparatus of the second embodiment:

Fig. 14 is a structural drawing of an apparatus of the third embodiment:

Fig. 15 is an explanatory drawing to show an example of a method for generating modulated light:

Fig. 16 is an explanatory drawing of the modulated light generated by the method shown in Fig 15

Fig. 17 is an explanatory drawing to show another example of the method for generating modulated light:

Fig. 18 is an explanatory drawing of the modulated light generated by the method shown in Fig. 17

Fig. 19 is an explanatory drawing to show still another example of the method for generating modulated light

Fig. 20 is an explanatory drawing of the modulated light generated by the method shown in Fig. 19: and

Fig. 21 is a structural drawing of an arithmetic processing unit for photodetection signals.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The principle of the present invention is first explained prior to the description of the embodiments of the present invention

[Principle of the Invention]

Let us consider a uniform scattering medium and suppose that light from a light source disposed on a surface of the scattering medium propagates inside the scattering medium and that photodetector disposed on the surface detects light escaping therefrom In this case the exterior shape of the scattering medium is arbitrary as long as it is comprised of faces which can prevent diffusing light from being again incident thereinto

Fig. 1 shows an example of a track of detected light (or a photon) propagated inside a scattering medium

The light is scattered by scattering particles. so that the optical path thereof is bent in a zigzag manner Then. the Lambert-Beer law holds for the zigzag flight pathlength ℓ and the intensity of the propagating light exponentially attenuates against the zigzag flight pathlength (cumulative distance) ℓ On this occasion. the flight pathlength is given as $\ell = ct$. where c is a speed of the light in the medium and t is a time-of-flight.

Furthermore. considering a time-resolved re-emission (waveform) J(ct) of a photodetection signal obtained by time-resolved measurement. the flight pathlength ℓ corresponds to the abscissa. $ct = \ell$. of the time-resolved re-emission (waveform) J(ct) of the photodetection signal. as shown in Fig. 2.

From the above. the following important relationships are obtained as to the flight pathlength and absorption of the zigzag light detected at time t. from which it is understood that the degree of absorption is associated with only the flight pathlength ℓ and absorption coefficient μ_a

$$ct = \ell = n\ell_s = n/\mu_s \tag{1}$$

$$\begin{aligned} J(ct) &= B_0 A(\mu_s', t)[\exp(-\mu_a/\mu_s)]^n \\ &= B_c A(\mu_s', t)\exp(-\mu_a \ell) \\ &= B_c A(\mu_s', t)\exp(-\mu_a ct) \end{aligned} \tag{2}$$

In the relationships.

ℓ_s the mean free pathlength. where $\ell_s = 1/\mu_s$.

n: the number of collisions with scattering particles.

μ_a: the absorption coefficient.

μ_s: the scattering coefficient.

μ_s': the transport scattering coefficient by similarity principle. $\mu_s' = (1 - g)\mu_s$ where g is the mean cosine of the scattering angle.

B_0: the intensity of light incident into the scattering medium.

$B_0A(\mu_s', t)$: a photodetection signal without absorption, that is, when $\mu_a = 0$

Here, $t >> t_s$, and $A(\mu_s', t)$ represents the effect of scattering.

Next derived are the basic relationships as to the behavior of the light inside the scattering medium from the above relationship. Consider a single photon to be incident at t=0 on a medium and $J(\mu_s', \mu_a, t)$ to be the probability density function for escape at a given time t for a single photon. First, for the time-resolved re-emission, which is an ensemble of photons (corresponding to the time-resolved measurement), the following relations hold.

$$J(\mu_s', \mu_a, t) = B_0A(\mu_s', t)\exp(-\mu_a ct) \tag{3}$$

$$\ln[J(\mu_s', \mu_a, t)] = -\mu_a ct + \ln[B_0A(\mu_s', t)] \tag{4}$$

$$(\partial/\partial\mu_a)J(\mu_s', \mu_a, t) = -ctB_0A(\mu_s', t)\exp(-\mu_a ct) \tag{5}$$

$$(\partial/\partial\mu_a)\ln[J(\mu_s', \mu_a, t)] = -ct \tag{6}$$

Here, formula (3) is a rewritten form of formula (2).

Among the above four formulas, formula (3) or (4) is convenient, for example, for quantification of concentration of hemoglobin in a living tissue. Namely, the effect of scattering can be eliminated by performing measurement with two kinds of light having different wavelengths at which the scattering coefficients are equal or regarded as equal, then obtaining $\ln J(\mu_s', \mu_a, t)$, and taking a ratio of values of $\ln J$ for the two wavelengths.

The inventor found out that because a quantity of detected light I is a time integration of the above $J(\mu_s', \mu_a, t)$, the following basic relations can be obtained as to the quantity of detected light I (a value of time integration, corresponding to CW measurement). A Laplace transform ($s = c\mu_a$) of $A(\mu_s', t)$ will be represented hereinafter by $F[A(\mu_s', t)]$

$$\begin{aligned} I(\mu_s', \mu_a) &= B_0\int_0^\infty A(\mu_s', t)\exp(-\mu_a ct)\,dt \\ &= B_0 F[A(\mu_s', t)] \end{aligned} \tag{7}$$

$$\ln[I(\mu_s', \mu_a)] = \ln B_0 + \ln[F[A(\mu_s', t)]] \tag{8}$$

$$(\partial/\partial\mu_a)I(\mu_s', \mu_a) = -B_0cF[tA(\mu_s', t)] \tag{9}$$

$$\begin{aligned} &(\partial/\partial\mu_a)\ln[I(\mu_s', \mu_a)] \\ &= -cF[tA(\mu_s', t)]/F[A(\mu_s', t)] \\ &= -c\langle t\rangle = -\langle L(\mu_a)\rangle \end{aligned} \tag{10}$$

$\langle L(\mu_a)\rangle$ in above formula (10) is equal to weighted mean $c\langle t\rangle$ of distribution of $J(\mu_s', \mu_a, t)$ in formula (3), which is called as a barycenter, average flight pathlength, or average optical pathlength.

This average flight pathlength $\langle L(\mu_a)\rangle$ can be calculated by arithmetic processing of time-resolved re-emission (waveform) $J(\mu_s', \mu_a', t)$ of detection signal. It can also be calculated by another method, for example from a phase delay of photodetection signal to incidence of modulated light. Since this average flight pathlength $\langle L(\mu_a)\rangle$ is a quantity obtainable by utilizing the whole of photodetection signal, that is, a quantity in the integral form, high signal-to-noise ratios (S/N) can be achieved. Generally, the average flight pathlength $\langle L(\mu_a)\rangle$ is dependent on μ_a.

The above is also verified by Monte Carlo simulation. The above description tells us that for utilizing photon diffusion equations, it is adequate to use a new diffusion constant D as defined by eliminating the absorption coefficient from the conventional diffusion constant. Namely, the new diffusion constant D is defined as follows.

$$D = 1/(3\mu_s') = 1/[3(1 - g)\mu_s] \tag{11}$$

The inventor of the present application first discloses the above views. These results and deduction therefrom do

not contradict with empirically obtained facts or views heretofore as far as the inventor of the present application knows

Then. the present invention further develops the above view: for example. formula (10) is expanded as follows First. the following formula is obtained from formula (10)

$$\ell n\, I\ (\mu_s'.\ \mu_a) = -\int_0^{\mu_a} <L\ (\mu_a)>\, d\mu_a + \ell n\, B_0 + C_0$$

$$= -G\ (\mu_a) + \ell n\, B_0 + C_0 \qquad (12)$$

Here. C_0 is an integration constant. and $G(\mu_a)$ is defined as follows.

$$G\ (\mu_a) = \int_0^{\mu_a} <L\ (\mu_a)>\, d\mu_a \qquad (13)$$

Supposing the scattering medium contains an absorptive constituent and $\in_1$. $\in_2$ represent absorption coefficients per unit concentration of the absorptive constituent for the respective kinds of light having the wavelengths λ_1 and λ_2. respectively. the concentration V of the absorptive constituent is given as follows.

$$V(\in_1 \cdot \in_2) = (\mu_{a1} \cdot \mu_{a2}) \qquad (14)$$

In the formula. μ_{a1} and μ_{a2} are the absorption coefficients of the absorptive constituent at wavelengths λ_1 and λ_2. respectively

Thus. assuming that the average flight pathlengths. $<L_1(\lambda_1)>$ and $<L_1(\lambda_2)>$. and the light quantities $I_1(\lambda_1) = I_1(\mu_{a1})$ and $I_1(\lambda_2) = I_1(\mu_{a2})$. are detected at a photodetection point r_1 for the incident light of the wavelength λ_1 (incident light intensity B_1) and the wavelength λ_2 (incident light intensity B_2) the following relation holds

$$\ell n\, \frac{I_1(\mu_{a1})}{I_1(\mu_{a2})} = G_1(\mu_{a2}) - G_1(\mu_{a1}) + \ell n\, \frac{B_1}{B_2}$$

$$= \int_{\mu_{a1}}^{\mu_{a2}} L_1(\mu_a)\, d\mu_a + \ell n\, \frac{B_1}{B_2} \qquad (15)$$

Accordingly. there exists ξ satisfying the following relation by the mean value theorem.

$$\ln[I_1(\lambda_1)/I_1(\lambda_2)] = (\mu_{a2} - \mu_{a1})L_1(\xi) + \ln[B_1/B_2] \qquad (16)$$

Here. $\mu_{a1} \leq \xi \leq \mu_{a2}$ or $\mu_{a1} \geq \xi \geq \mu_{a2}$

On the other hand. $L_1(\xi)$ can be expressed as follows using the average flight pathlengths. $<L_1(\lambda_1)>$ and $<L_1(\lambda_2)>$.

$$L_1(\xi) = p<L_1(\lambda_1)> + (1 - p)<L_1(\lambda_2)> \qquad (17)$$

Here. p is an appropriate value to satisfy the condition of $0 \leq p \leq 1$.

The inventor thus found out that if $B_1 = B_2$ the concentration V of the absorptive constituent can be calculated according to the following formula.

$$V = (\epsilon_2 - \epsilon_1)^{-1}[L_1(\xi)]^{-1} \times \ln[I_1(\lambda_1)/I_1(\lambda_2)]$$

$$= (\epsilon_2 - \epsilon_1)^{-1} \times [p<L_1(\lambda_1)> + (1 - p)<L_1(\lambda_2)>]^{-1}$$

$$\times \ln[I_1(\lambda_1)/I_1(\lambda_2)] \qquad (18)$$

Here. because $\in_2$ and $\in_1$ are known quantities. the concentration V of a specific absorptive constituent can be calculated from the values obtained by measurement. that is. from the average flight pathlengths $<L_1(\lambda_1)>$ and $<L_1(\lambda_2)>$. the light quantities $\ln I_1(\lambda_1)$ and $\ln I_1(\lambda_2)$. and the value of p that can be empirically determined.

In actual measurement, sufficient measurement accuracy can be achieved using $p = 1/2$ and an average value of $\langle L_1(\lambda_1)\rangle$ and $\langle L_1(\lambda_2)\rangle$ for $L(\xi)$ as follows.

$$L(\xi) = (1/2)[\langle L_1(\lambda_1)\rangle + \langle L_1(\lambda_2)\rangle] \quad (19)$$

More generally, the inventor found out that if $B_1 \neq B_2$ and if photodetection is carried out at photodetection points r_1 and r_2 for the incident light of the wavelength λ_1 (incident light intensity B_1) and the wavelength λ_2 (incident light intensity B_2) to detect the average flight pathlengths $\langle L_1(\lambda_1)\rangle$, $\langle L_1(\lambda_2)\rangle$, $\langle L_2(\lambda_1)\rangle$, $\langle L_2(\lambda_2)\rangle$ and the light quantities $I_1(\lambda_1)$, $I_1(\lambda_2)$, $I_2(\lambda_1)$, $I_2(\lambda_2)$, the concentration V of the absorptive constituent can be calculated according to the following formula.

$$\begin{aligned} V &= (\epsilon_2 - \epsilon_1)^{-1}[L_1(\xi_1) - L_2(\xi_2)]^{-1} \\ &\times \ln\{[I_1(\lambda_1)I_2(\lambda_2)]/[I_1(\lambda_2)I_2(\lambda_1)]\} \\ &= (\epsilon_2 - \epsilon_1)^{-1} \times [p\langle L_1(\lambda_1)\rangle + (1-p)\langle L_1(\lambda_2)\rangle \\ &- q\langle L_2(\lambda_1)\rangle - (1-q)\langle L_2(\lambda_2)\rangle]^{-1} \\ &\times \ln\{[I_1(\lambda_1)I_2(\lambda_2)]/[I_1(\lambda_2)I_2(\lambda_1)]\} \end{aligned} \quad (20)$$

Here, p is an appropriate value to satisfy the condition of $0 \leq p \leq 1$ and q is an appropriate value to satisfy the condition of $0 \leq q \leq 1$.

Also in this case, similarly as in the above case because ϵ_2 and ϵ_1 are known quantities, the concentration V of a specific absorptive constituent can be calculated from the values obtainable by measurement, that is, the average flight pathlengths $\langle L_1(\lambda_1)\rangle$, $\langle L_1(\lambda_2)\rangle$, $\langle L_2(\lambda_1)\rangle$, $\langle L_2(\lambda_2)\rangle$ the light quantities $\ln I_1(\lambda_1)$, $\ln I_1(\lambda_2)$, $\ln I_2(\lambda_1)$, $\ln I_2(\lambda_2)$, and the values of p and q that can be empirically determined.

Further, sufficient measurement accuracy can also be achieved in this case using the following.

$$L_1(\xi_1) - L_2(\xi_2) = (1/2)[\langle L_1(\lambda_1)\rangle + \langle L_1(\lambda_2)\rangle - \langle L_2(\lambda_1)\rangle - \langle L_2(\lambda_2)\rangle] \quad (21)$$

If a scattering medium contains two absorptive constituents, measurement should be done with light including three wavelengths. Supposing concentrations of the two absorptive constituents are V_1, V_2, two simultaneous equations hold for V_1 and V_2 like formula (18) or (20). Accordingly V_1 and V_2 can be obtained by solving the simultaneous equations. More generally, if a scattering medium contains m absorptive constituents, concentrations of the m absorptive constituents can be measured using light of (m + 1) wavelengths.

For example, Fig. 3 shows absorption spectra of oxygenated hemoglobin and deoxygenated hemoglobin and oxygenated myoglobin and deoxygenated myoglobin. It is important, for example, to measure a ratio of an oxygenated component and a deoxygenated component as to hemoglobin in the brain. In this case, measurement according to the above-discussed principle can be applied utilizing light of wavelengths to show a great difference in absorption coefficient between the oxygenated component and the deoxygenated component, namely using the light of wavelengths in the range of 700 nm to 1.2 μm.

In the above description, the scattering coefficients of scattering constituents for the respective kinds of light having different wavelengths are equal to each other or regarded a difference between them as very small, if any. For actual living samples, the wavelengths can be selected so as to minimize the difference to the ignorable extent.

The above description clarified the method for measuring the concentration of a specific absorptive constituent for a variety of scattering media in different shapes. Now, embodiments of the present invention are explained below with reference to the accompanying drawings. In the following description with the drawings, same elements will be denoted by same reference numerals, and redundant description will be omitted.

(First Embodiment)

Fig. 4 shows the first embodiment of the present invention and illustrates a method and apparatus arrangement for measuring a concentration of an absorptive constituent inside a scattering medium 20. This arrangement provides eight parameter values associated with light of two wavelengths (λ_1, λ_2) and two photodetection distances (r_1, r_2), and thus, the concentration of the absorptive constituent can be measured according to formula (20) discussed above.

A light source 2 is a laser diode, which emits pulsed light (pulsed light beams) of different wavelengths λ_1 and λ_2. The time width of the pulsed light can be freely selected normally in the range of about 10 ps to 100 ns as long as it is short enough to allow derivation of average flight pathlengths from a photodetection signal. Further, the wavelengths of

light need properly be selected depending upon an object to be measured. Generally, light of above 700 nm is often used for living samples because of absorption of hemoglobin and the like. The light source may be a light-emitting diode, a HeNe laser, etc. in addition to the laser diode.

The pulsed light beams from the light source 2 are subjected to wavelength selection in a wavelength selector 4 and either pulsed light beam of the selected wavelength is selectively guided through a light guide 6 to be made incident into the surface of the scattering medium 20, which is the measured object. In this case, another method for making pulsed light beams of two wavelengths simultaneously incident into the surface of the scattering medium may be employed, and in that case the wavelength selector 4 is omitted.

A space between the light guide 6 and the scattering medium 20 is kept fine enough in the embodiment of Fig. 4. In actual applications, this space, however, may be expanded as filled with a liquid material or a jelly material (hereinafter referred to as an interface material) having a refractive index and a scattering coefficient nearly equal to those of the scattering medium 20. Namely, such an arrangement will raise no problem because the light diffusively propagates in the interface material to enter the measured object. In the cases where surface reflection of the scattering medium is problematic, the effect of the surface reflection etc. can be reduced by properly selecting the interface material.

The light diffusively having propagated through inside the scattering medium is received by light guides 8 and 9 placed at positions apart distances r_1 and r_2, respectively, from the position of incidence of the light. The interface material may be used here as well from the same reason as above.

First photodetector 12 and second photodetector 13 convert the optical signals into electric signals, amplify them if necessary, and then output respective photodetection signals. The photodetectors 12 and 13 may be selected from photomultiplier tubes, phototubes, photodiodes, avalanche photodiodes, PIN photodiodes, etc. Any photodetector may be selected as long as it owns spectral sensitivity characteristics for detecting the light of the predetermined wavelengths and a time response speed required. If the optical signals are weak, high-gain photodetectors are to be used. Further, photons may be counted by the time correlation photon counting method. The other portions of the photodetectors than the light-receiving surfaces are desired to be arranged to absorb or shield the light. In the cases where the pulsed light beams of two wavelengths are made simultaneously incident into the scattering medium as described previously, it is preferred that appropriate wavelength selection filters (not shown) be interposed one between the photodetector 12 and the scattering medium 20 and the other between the photodetector 13 and the scattering medium 20.

A parameter detection unit 15 detects light quantities and average flight pathlengths from above photodetection signals. Since a light quantity is a time integration value of a photodetection signal, it can be readily obtained by integrating the photodetection signal. Since an average flight pathlength is a weighted mean of time-resolved re-emission (waveform) of a photodetection signal obtained for a short light-pulse incidence, it can be readily obtained by executing, for example, the arithmetic processing of formula (10) described previously, or arithmetic processing equivalent thereto from the time-resolved re-emission (waveform) of the photodetection signal. In this case, the parameter detection unit utilizes, with necessity, signals synchronized with generation of light pulses of the light source 2.

An arithmetic processing unit 16 calculates the concentration V of the absorptive constituent, based on the previous formula (20), using the eight parameter values obtained in the parameter detection unit, i.e., the light quantities $I_1(\lambda_1)$, $I_1(\lambda_2)$ and the average flight pathlengths $\langle L_1(\lambda_1)\rangle$, $\langle L_1(\lambda_2)\rangle$ at the position r_1 for incidence of the pulsed light of the wavelengths λ_1 and λ_2, and the light quantities $I_2(\lambda_1)$, $I_2(\lambda_2)$ and the average flight pathlengths $\langle L_2(\lambda_1)\rangle$, $\langle L_2(\lambda_2)\rangle$ at the position r_2 for incidence of the pulsed light of the wavelengths λ_1 and λ_2. On this occasion, the processing unit uses the constants p and q which can be empirically determined. In actual measurement, sufficient accuracy is achieved with $p = q = 1/2$. The arithmetic processing is carried out at high speed, for example, by a microcomputer incorporated in the arithmetic processing unit.

If incident light intensities of the wavelengths λ_1 and λ_2, in the pulsed light into the scattering medium 20 are equal to each other, or can be controlled so as to become equal to each other or become a predetermined ratio previously known, the second photodetector 13 can be omitted. In this case, the parameter detection unit 15 obtains four parameters, the light quantities $I_1(\lambda_1)$, $I_1(\lambda_2)$ and the average flight pathlengths $\langle L_1(\lambda_1)\rangle$ and $\langle L_1(\lambda_2)\rangle$ at the position r_1 for incidence of the pulsed light of the wavelengths λ_1 and λ_2. Accordingly, the arithmetic processing unit 16 calculates the concentration V of the absorptive constituent, based on the above formula (18), using these parameter values. On this occasion, the processing unit uses the constant p that can be empirically determined, but in actual measurement, sufficient accuracy can be achieved with $p = 1/2$. The arithmetic processing is executed at high speed, for example, by the microcomputer incorporated in the arithmetic processing unit.

The above description illustrated the method in which the light was made incident at a position and it was detected at two points different therefrom. It is, however, clear that in actual applications light beams of different wavelengths may be made incident at two positions and these light beams may be detected in parallel or in time division at another point or other points.

As described above, the above embodiment may employ either the method using the light including beams of different wavelengths made incident or the method using the light beams of different wavelengths made incident in time division. The former may employ a method arranged to make the light beams of different wavelengths in concentric

beams and to wavelength-select the light beams by a wavelength selection filter provided immediately before the position of incidence of light. a method arranged to make the light beams incident into the scattering medium as they are and to wavelength-select the light beams by a wavelength selection filter provided immediately before the photodetector. or a method arranged to split each detected light into two beams. to wavelength-select each of the two beams. and to detect the beams by totally four photodetectors in parallel. The latter may utilize a light beam switch using a mirror on the light source side. a wavelength switch using a filter. or a light switch using an optical switch.

The means for guiding the light into the scattering medium may be a method using a condenser lens (Fig. 5). a method using an optical fiber (Fig. 6). a method utilizing a pinhole (Fig. 7). or a method for guiding the light into a body to apply it from inside. such as a gastrocamera (Fig. 8). in place of the optical guide shown in Fig 4. Also. the light may be made incident in the form of a thick beam into the scattering medium. This case may be considered as a plurality of spot light sources arranged in the beam.

The means for detecting the light diffusively having propagated inside the scattering medium may be a method for directly detecting the light (Fig. 9). a method using an optical fiber (Fig. 10). or a method using a lens (Fig. 11). in addition to the method using the light guide shown in Fig. 4.

If the first embodiment as described above is arranged to use the light of three wavelengths. it can measure concentrations of two absorptive constituents in a scattering medium containing the two absorptive constituents or a concentration of one absorptive constituent in a scattering medium containing a lot of absorptive constituents and a total concentration of the other absorptive constituents. For example. oxygenated hemoglobin and deoxygenated hemoglobin have different absorption coefficients depending upon the wavelengths. as shown in Fig. 3 in the previous description Therefore. concentrations of those and oxygen saturation can be measured using the light of three wavelengths properly selected. Generally. concentrations of m absorptive constituents can be measured using light of (m + 1) wavelengths In addition the measurement accuracy can be improved using light of wavelengths of more than (m + 1).

If the above measurement is carried out at different times. a time change of concentration of absorptive constituent can be measured. Further. a spatial distribution of concentration can be measured by synchronous scanning (not shown) of the position of incidence of light and positions of photodetection with respect to the scattering medium and measuring concentrations of the absorptive constituent in respective portions of the scattering medium. The arithmetic processing unit 16 has a function to store concentration information of absorptive constituent thus obtained. and a display recording unit 18 displays or records the information.

The arithmetic processing can be executed at high speed by a computer device provided with a memory and a display

(Second Embodiment)

Fig. 12 shows the second embodiment of the present invention to illustrate a method and apparatus arrangement for measuring or monitoring a concentration of oxygenated hemoglobin or oxygen saturation of hemoglobin (a ratio between a concentration of oxygenated hemoglobin to a concentration of overall hemoglobin) inside a scattering medium 30 such as a human head. This embodiment can measure the concentration of oxygenated hemoglobin and the oxygen saturation of hemoglobin by substituting twelve parameter values obtained using the light of three wavelengths (λ_1. λ_2. λ_3) and two photodetection distances (r_1. r_2) into three simultaneous equations based on formula (20) as discussed previously.

A container 26 with a mount band is mounted on the head 30 like a headband. The apparatus shown in this embodiment uses the light of three predetermined wavelengths λ_1. λ_2. and λ_3. and the operation thereof is substantially the same as that of the apparatus of the first embodiment. Fig. 13 shows a part of the apparatus arrangement shown in Fig. 12. that is. the details of the inside of the container 26.

In Fig. 13. pulsed light (pulsed light beams) of the predetermined wavelengths λ_1. λ_2. and λ_3 emitted from the light source 2 is subjected to wavelength selection in the wavelength selector 4 and each light beam of the selected wavelength is selectively guided through the light guide 6 into the head 30. On this occasion. the three wavelengths are properly selected by reference to the absorption spectra of hemoglobin shown in previous Fig. 3.

The light diffusively having propagated through inside the head is received by the light guides 8 and 9 placed at positions apart distances r_1 and r_2. respectively. from the position of incidence of the light. and the first photodetector 12 and second photodetector 13 convert the light into electric signals and amplify the signals if necessary. The signals obtained herein are those for the three wavelengths and the two photodetection distances. The power supply and various signals are connected through a connector 28 attached to the container 26 to an external device 34 by a signal cable 32. A parameter detection unit (not shown) in the external device 34 obtains light quantities and average flight pathlengths for the three wavelengths and two photodetection distances. i.e. twelve parameters.

On this occasion, two simultaneous equations. similar to previous formula (20). hold for the signals obtained as to the wavelengths λ_1 and λ_2 and the signals obtained as to the wavelengths λ_1 and λ_3. Accordingly, similarly as in the first embodiment. the arithmetic processing unit (not shown) can calculate the concentration V_1 of oxygenated hemo-

are not to be regarded as a departure from the spirit and scope of the invention. and all such modifications as would be obvious to one skilled in the art are intended to be included within the scope of the following claims.

The basic Japanese Application No.228253/1994 filed on September 22. 1994 is hereby incorporated by reference

Claims

1. A method for measuring a concentration of an absorptive constituent in a scattering medium. comprising:

   (a) a step of emitting two or more kinds of light having predetermined wavelengths. at which scattering coefficients are equal or regarded as equal. toward a scattering medium which is a measured object:

   (b) a step of making said light incident at a light incidence position into said scattering medium and letting said light propagate through said scattering medium:

   (c) a step of detecting said light having propagated through said scattering medium at one or more photodetection points different from said light incidence position. thereby acquiring one or more photodetection signals.

   (d) a step of detecting light quantities and average flight pathlengths at said one or more photodetection points for said respective kinds of light having said wavelengths. based on said one or more photodetection signals. and

   (e) a step of obtaining a concentration of said absorptive constituent by arithmetic processing using said light quantities and said average flight pathlengths. based on a predetermined relationship among said light quantities said average flight pathlengths. and a difference between absorption coefficients per unit concentration of said absorptive constituent. for said respective kinds of light having said wavelengths

2. The method according to Claim 1. wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of pulsed light.

3. The method according to Claim 1. wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of sinusoidally modulated light having a predetermined modulation frequency component.

   wherein said light quantities are calculated from amplitudes of said predetermined modulation frequency component included in said photodetection signals and

   wherein said average flight pathlengths are calculated from phase delays of said predetermined modulation frequency component

4. The method according to Claim 1. wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of sinusoidally modulated light having a predetermined modulation frequency component.

   wherein said light quantities are calculated from dc components of said photodetection signals. and

   wherein said average flight pathlengths are calculated from phase delays of said predetermined modulation frequency component included in said photodetection signals.

5. The method according to Claim 1. wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of modulated light having a predetermined repetitive modulation frequency component.

   wherein said light quantities are calculated from amplitudes of said predetermined repetitive modulation frequency component or a frequency component of an integral multiple thereof included in said photodetection signals. and

   wherein said average flight pathlengths are calculated from phase delays of said predetermined repetitive modulation frequency component or the frequency component of the integral multiple thereof.

6. The method according to Claim 1. wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of modulated light having a predetermined repetitive modulation frequency component.

   wherein said light quantities are calculated from dc components of said photodetection signals. and

   wherein said average flight pathlengths are calculated from phase delays of said predetermined repetitive modulation frequency component or a frequency component of an integral multiple thereof included in said photodetection signals.

7. The method according to Claim 1. wherein said predetermined relationship among said light quantities. said average

flight pathlengths. and said difference between the absorption coefficients per unit concentration of said absorptive constituent. for said respective kinds of light having said wavelengths. is a relationship derived from that a partial differentiation of a natural logarithm of a light quantity detected with respect to an absorption coefficient is equal to an average flight pathlength.

8. The method according to Claim 1. wherein said step (e) comprises obtaining the concentration of the absorptive constituent in said scattering medium by arithmetic processing using said light quantities and said average flight pathlengths. based on a relationship expressed by the following formula:

$$V = (\in_2 - \in_1)^{-1} \times [p<L_1(\lambda_1)> + (1 - p)<L_1(\lambda_2)>]^{-1} \times \ln[I_1(\lambda_1)/I_1(\lambda_2)]$$

where

V: the concentration of the absorptive constituent.

$\in_1$: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1.

$\in_2$: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2.

$<L_1(\lambda_1)>$: the average flight pathlength for the light of the wavelength λ_1 at a photodetection point r_1.

$<L_1(\lambda_2)>$: the average flight pathlength for the light of the wavelength λ_2 at the photodetection point r_1.

$I_1(\lambda_1)$: the quantity of detected light for the light of the wavelength λ_1 at the photodetection point r_1

$I_1(\lambda_2)$: the quantity of detected light for the light of the wavelength λ_2 at the photodetection point r_1. and

p. a predetermined value satisfying $0 < p < 1$

9. The method according to Claim 1 wherein said step (e) comprises obtaining the concentration of the absorptive constituent in said scattering medium by arithmetic processing using said light quantities and said average flight pathlengths. based on a relationship expressed by the following formula:

$$V = (\in_2 - \in_1)^{-1} \times [p<L_1(\lambda_1)> + (1 - p)<L_1(\lambda_2)> - q<L_2(\lambda_1)> - (1 - q)<L_2(\lambda_2)>]^{-1}$$

$$\times \ln\{[I_1(\lambda_1)\cdot I_2(\lambda_2)]/[I_1(\lambda_2)\cdot I_2(\lambda_1)]\}$$

where

V the concentration of the absorptive constituent.

$\in_1$ the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1.

$\in_2$ the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2.

$<L_1(\lambda_1)>$ the average flight pathlength at a photodetection point r_1 for the light of the wavelength λ_1.

$<L_1(\lambda_2)>$: the average flight pathlength at the photodetection point r_1 for the light of the wavelength λ_2.

$<L_2(\lambda_1)>$: the average flight pathlength at a photodetection point r_2 for the light of the wavelength λ_1.

$<L_2(\lambda_2)>$: the average flight pathlength at the photodetection point r_2 for the light of the wavelength λ_2.

$I_1(\lambda_1)$: the quantity of detected light at the photodetection point r_1 for the light of an intensity B_1 and the wavelength λ_1.

$I_1(\lambda_2)$ the quantity of detected light at the photodetection point r_1 for the light of an intensity B_2 and the wavelength λ_2.

$\lambda_2(\lambda_1)$: the quantity of detected light at the photodetection point r_2 for the light of the intensity B_1 and the wavelength λ_1.

$I_2(\lambda_2)$: the quantity of detected light at the photodetection point r_2 for the light of the intensity B_2 and the wavelength λ_2.

p: a predetermined value satisfying $0 \leq p \leq 1$. and

q: a predetermined value satisfying $0 < q < 1$.

10. An apparatus for measuring a concentration of an absorptive constituent in a scattering medium. comprising:

(a) a light source for emitting two or more kinds of light having predetermined wavelengths. at which scattering coefficients are equal or regarded as equal. toward a scattering medium which is a measured object:

(b) light incidence means for making said light incident at a light incidence position into said scattering medium and making said light propagate through said scattering medium:

(c) photodetection means for detecting said light having propagated through said scattering medium, at one or more photodetection points different from said light incidence position to acquire one or more photodetection signals;

(d) parameter detecting means for detecting light quantities and average flight pathlengths at said one or more photodetection points for said respective kinds of light having said wavelengths, based on said one or more photodetection signals; and

(e) arithmetic processing means for obtaining a concentration of said absorptive constituent by arithmetic processing using said light quantities and said average flight pathlengths, based on a predetermined relationship among said light quantities, said average flight pathlengths, and a difference between absorption coefficients per unit concentration of said absorptive constituent, for said respective kinds of light having said wavelengths.

11. The apparatus according to Claim 10, wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of pulsed light.

12. The apparatus according to Claim 10, wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of sinusoidally modulated light having a predetermined modulation frequency component

wherein said light quantities are calculated from amplitudes of said predetermined modulation frequency component included in said photodetection signals, and

wherein said average flight pathlengths are calculated from phase delays of said predetermined modulation frequency component

13. The apparatus according to Claim 10, wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of sinusoidally modulated light having a predetermined modulation frequency component,

wherein said light quantities are calculated from dc components of said photodetection signals, and

wherein said average flight pathlengths are calculated from phase delays of said predetermined modulation frequency component included in said photodetection signals.

14. The apparatus according to Claim 10 wherein said two or more kinds of light having predetermined wavelengths are two or more Kinds of modulated light having a predetermined repetitive modulation frequency component,

wherein said light quantities are calculated from amplitudes of said predetermined repetitive modulation frequency component or a frequency component of an integral multiple thereof included in said photodetection signals, and

wherein said average flight pathlengths are calculated from phase delays of said predetermined repetitive modulation frequency component or the frequency component of the integral multiple thereof

15. The apparatus according to Claim 10, wherein said two or more kinds of light having predetermined wavelengths are two or more kinds of modulated light having a predetermined repetitive modulation frequency component,

wherein said light quantities are calculated from dc components of said photodetection signals, and

wherein said average flight pathlengths are calculated from phase delays of said predetermined repetitive modulation frequency component or a frequency component of an integral multiple thereof included in said photodetection signals.

16. The apparatus according to Claim 10, wherein said predetermined relationship among said light quantities, said average flight pathlengths, and said difference between the absorption coefficients per unit concentration of said absorptive constituent, for said respective kinds of light having said wavelengths, is a relationship derived from that a partial differentiation of a natural logarithm of a light quantity detected with respect to an absorption coefficient is equal to an average flight pathlength

17. The apparatus according to Claim 10, wherein said arithmetic processing means (e) obtains the concentration of the absorptive constituent in said scattering medium by arithmetic processing using said light quantities and said average flight pathlengths, based on a relationship expressed by the following formula:

$$V = (\epsilon_2 - \epsilon_1)^{-1} \times [p\langle L_1(\lambda_1)\rangle + (1 - p)\langle L_1(\lambda_2)\rangle]^{-1} \times \ln[I_1(\lambda_1)/I_1(\lambda_2)]$$

where

V: the concentration of the absorptive constituent.

$\in_1$: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1.

$\in_2$: the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2.

$<L_1(\lambda_1)>$: the average flight pathlength for the light of the wavelength λ_1 at a photodetection point r_1.

$<L_1(\lambda_2)>$ the average flight pathlength for the light of the wavelength λ_2 at the photodetection point r_1

$I_1(\lambda_1)$: the quantity of detected light for the light of the wavelength λ_1 at the photodetection point r_1.

$I_1(\lambda_2)$: the quantity of detected light for the light of the wavelength λ_2 at the photodetection point r_1, and

p: a predetermined value satisfying $0 \leq p \leq 1$.

18. The apparatus according to Claim 10, wherein said arithmetic processing means (e) obtains the concentration of the absorptive constituent in said scattering medium by arithmetic processing using said light quantities and said average flight pathlengths, based on a relationship expressed by the following formula:

$$V = (\in_2 - \in_1)^{-1} \times [p<L_1(\lambda_1)> + (1 - p<L_1(\lambda_2)> - q(L_2(\lambda_1)> - (1 - q)<L_2(\lambda_2)>]^{-1}$$

$$\times \ln\{[I_1(\lambda_1)\cdot I_2(\lambda_2)]/[I_1(\lambda_2)\cdot I_2(\lambda_1)]\}$$

where

V: the concentration of the absorptive constituent.

$\in_1$ the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_1.

$\in_2$ the absorption coefficient per unit concentration of the absorptive constituent for the light of the wavelength λ_2.

$<L_1(\lambda_1)>$ the average flight pathlength at a photodetection point r_1 for the light of the wavelength λ_1

$(L_1(\lambda_2)$: the average flight pathlength at the photodetection point r_1 for the light of the wavelength λ_2.

$<L_2(\lambda_1)>$: the average flight pathlength at a photodetection point r_2 for the light of the wavelength λ_1.

$<L_2(\lambda_2)>$ the average flight pathlength at the photodetection point r_2 for the light of the wavelength λ_2.

$I_1(\lambda_1)$: the quantity of detected light at the photodetection point r_1 for the light of an intensity B_1 and the wavelength λ_1.

$I_1(\lambda_2)$: the quantity of detected light at the photodetection point r_1 for the light of an intensity B_2 and the wavelength λ_2.

$I_2(\lambda_1)$: the quantity of detected light at the photodetection point r_2 for the light of the intensity B_1 and the wavelength λ_1.

$I_2(\lambda_2)$ the quantity of detected light at the photodetection point r_2 for the light of the intensity B_2 and the wavelength λ_2.

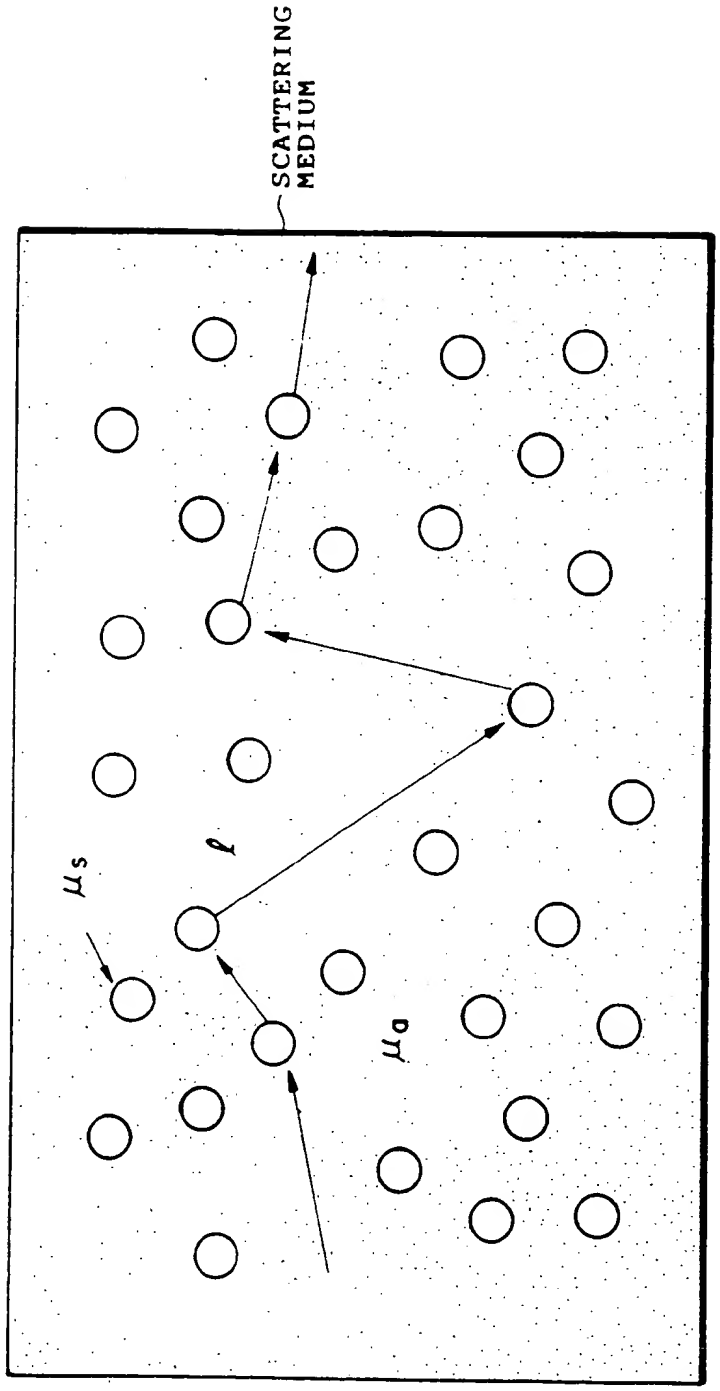
p a predetermined value satisfying 0 p 1, and

q a predetermined value satisfying 0 q 1

19. Use of the apparatus according to any one of claims 10 to 18 for measuring a concentration of an absorptive constituent in a scattering medium.

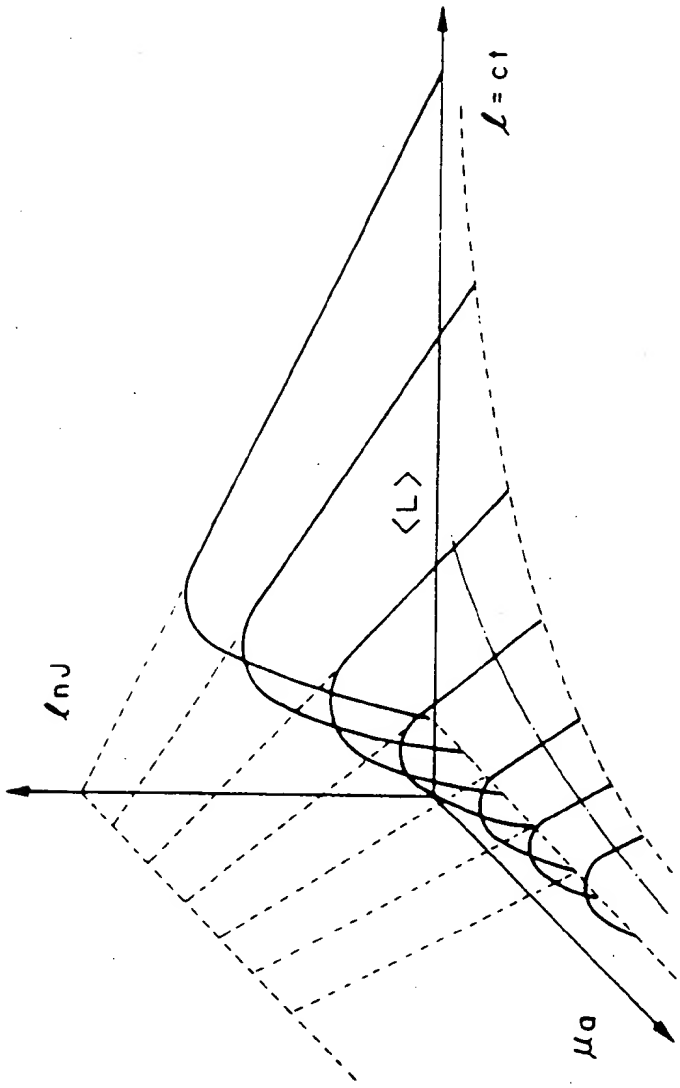
20. A method and apparatus for measuring a characteristic of a light scattering medium, wherein a plurality of different kinds of light which will behave similarly in a selected scattering medium are directed toward the scattering medium and light from the scattering medium is analysed to determine the characteristic of the medium.

Fig. 1



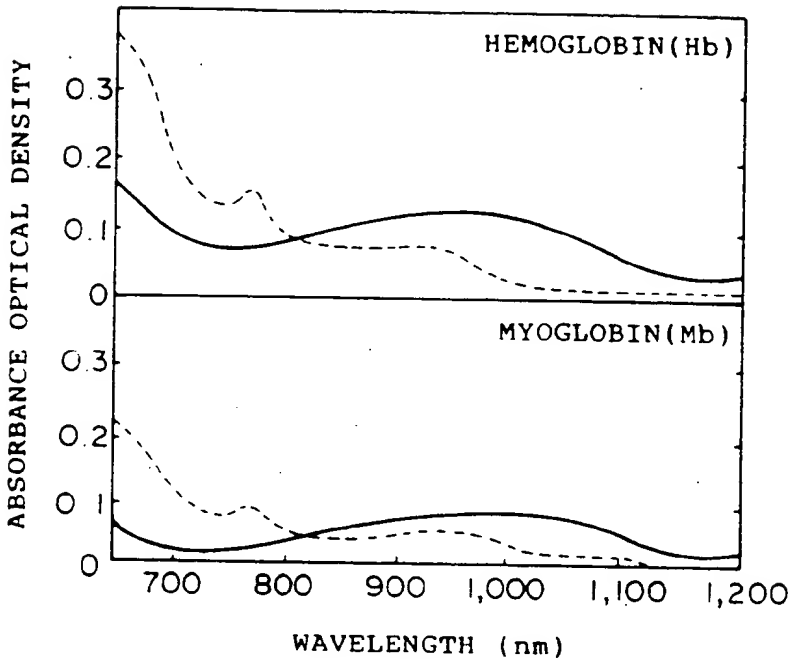
TRACK OF LIGHT TRANSMITTED IN SCATTERING MEDIUM

Fig. 2



EXAMPLE OF TIME - RESOLVED RE-EMISSION

Fig. 3

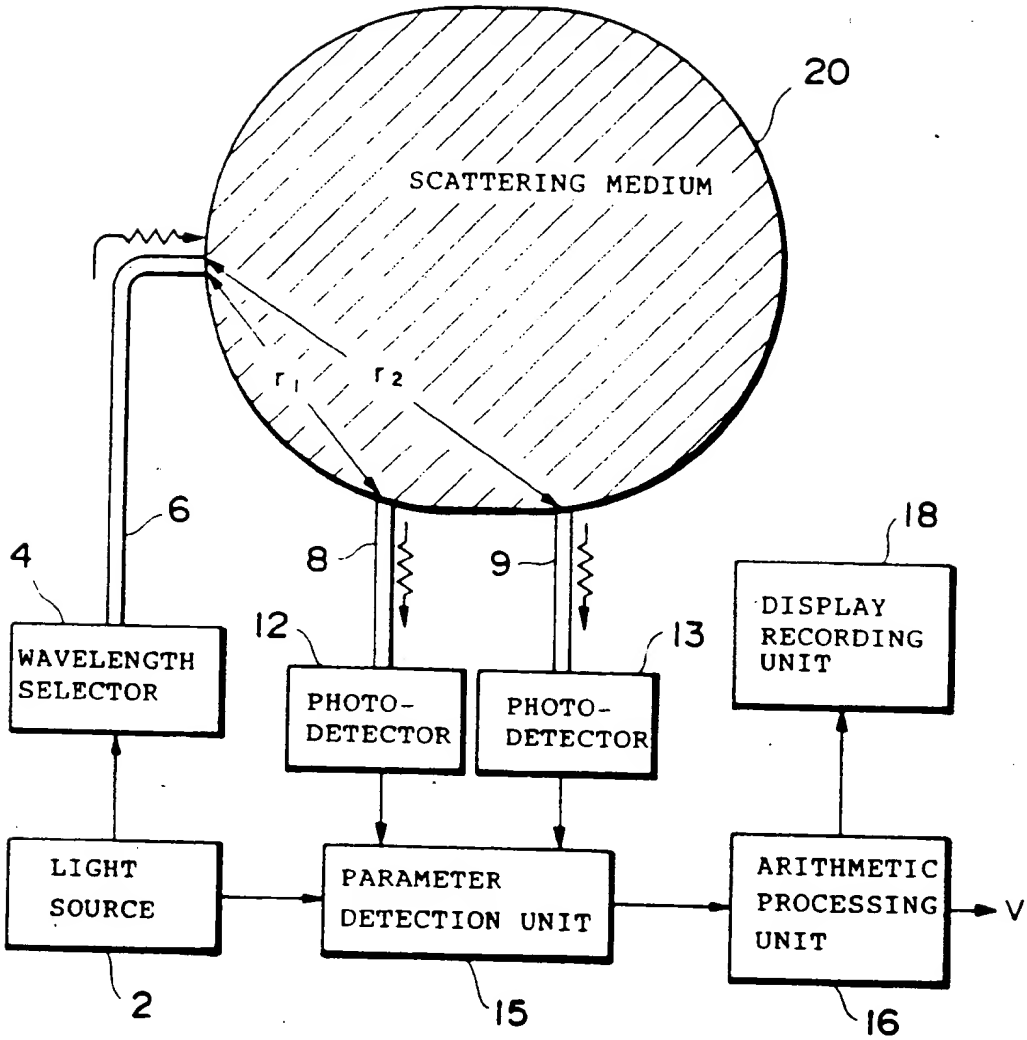


NEAR-INFRARED ABSORPTION SPECTRA OF Hb(0.37mM) AND Mb(0.15mM)

ABSOLUTE SPECTRUM
SOLID LINE:OXYGENATED
DOTTED LINE:DEOXYGENATED

ABSORPTION SPECTRA OF VARIOUS BIOLOGICAL MATERIALS

Fig. 4



STRUCTURE OF APPARATUS OF THE FIRST EMBODIMENT

Fig. 5

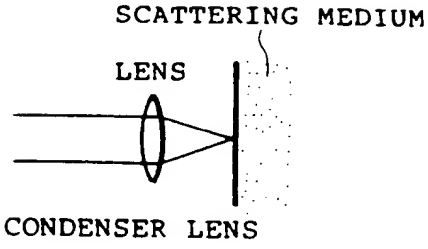


Fig. 6

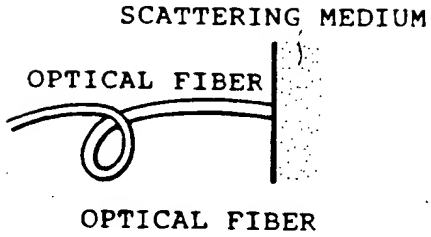


Fig. 7

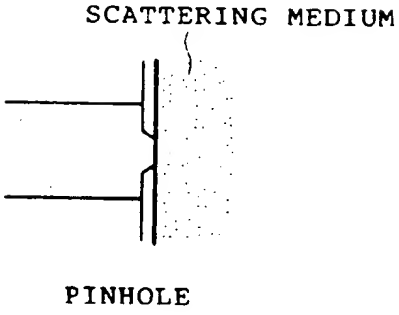
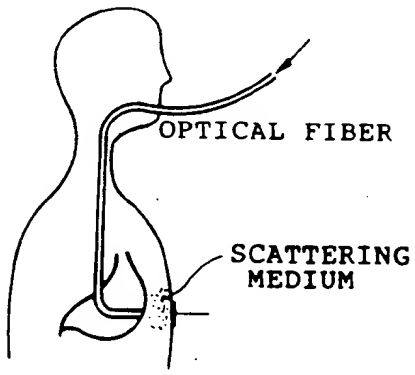
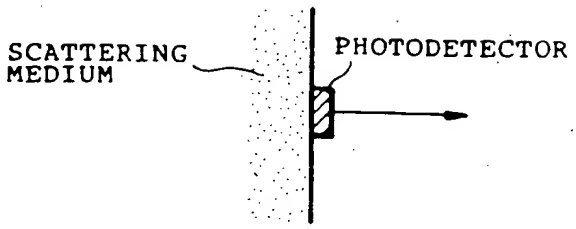


Fig. 8



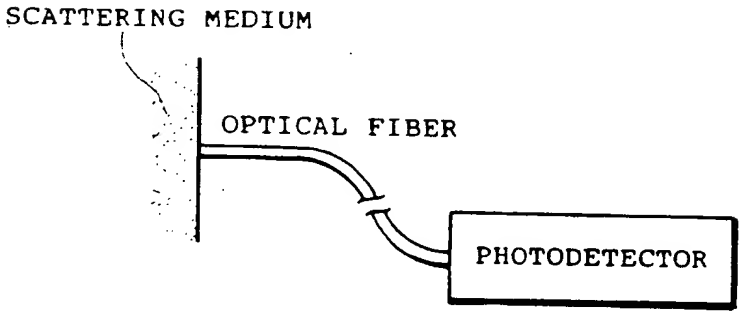
LIGHT INCIDENCE FROM THE INSIDE OF SCATTERING MEDIUM

Fig. 9



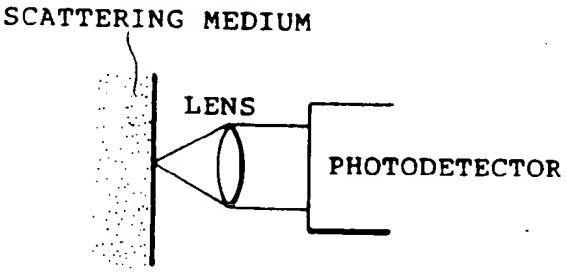
DIRECT DETECTION

Fig. 10



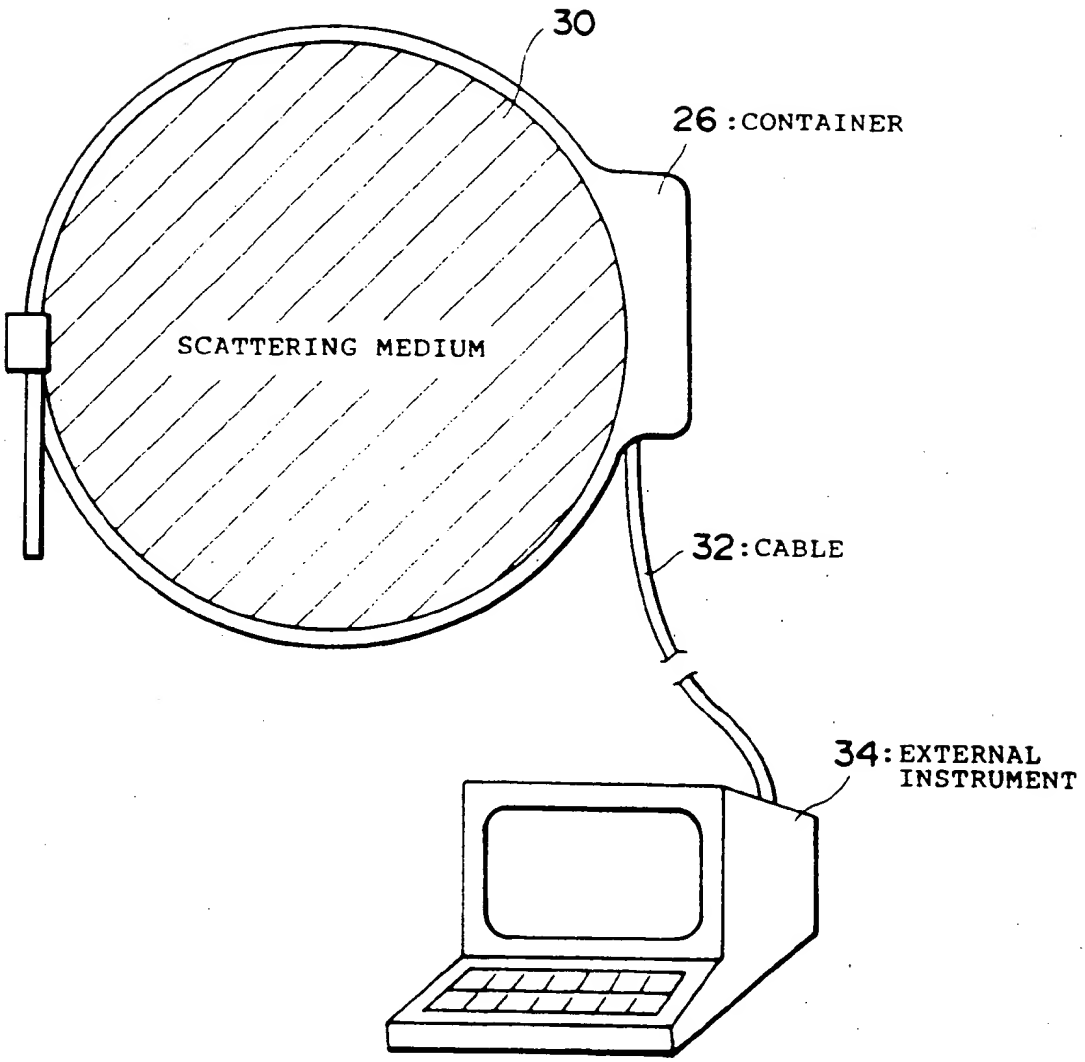
OPTICAL FIBER

Fig. 11



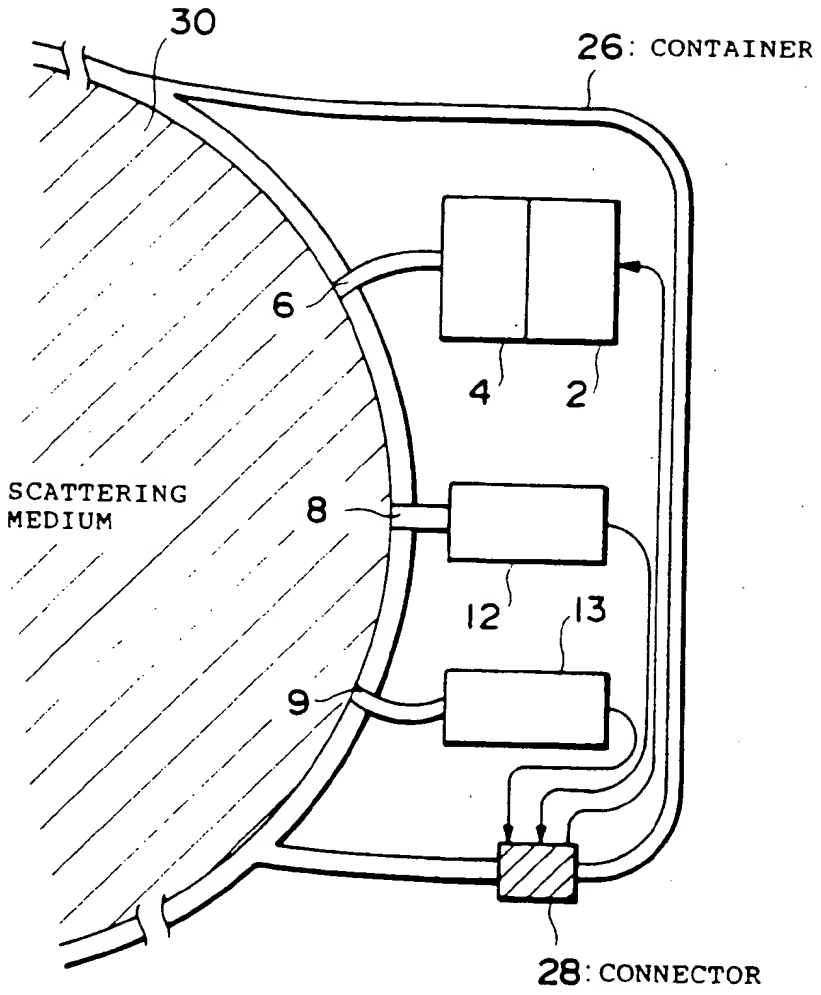
LENS COUPLING

Fig. 12



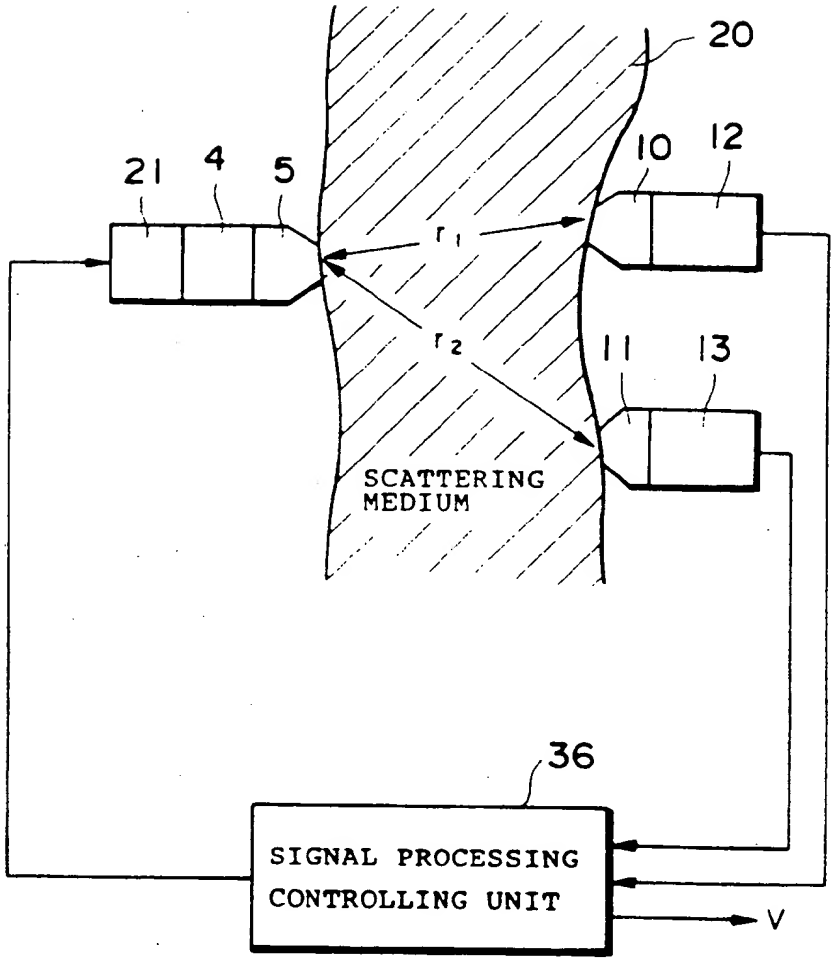
STRUCTURE OF APPARATUS OF THE SECOND EMBODIMENT

Fig. 13



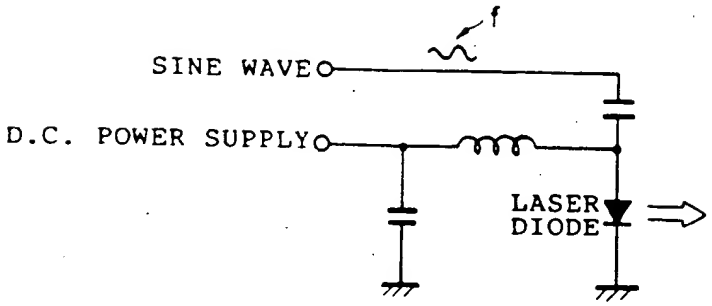
CONFIGURATION OF A LIGHT INCIDENCE POSITION AND PHOTODETECTION POINTS OF THE APPARATUS OF THE SECOND EMBODIMENT

Fig. 14



STRUCTURE OF APPARATUS OF THE THIRD EMBODIMENT

Fig. 15



METHOD FOR GENERATING MODULATED LIGHT WITH A LASER DIODE

Fig. 16

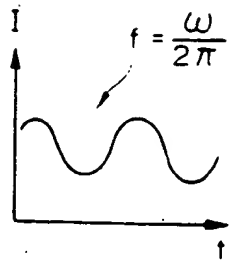
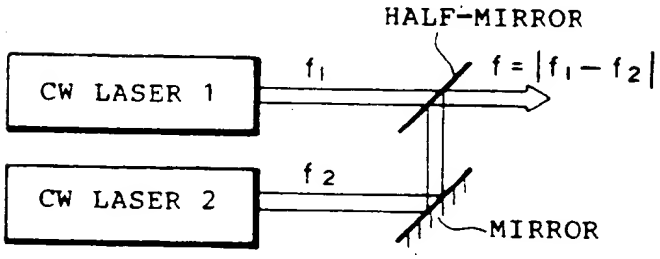


Fig. 17



METHOD FOR GENERATING MODULATED LIGHT UTILIZING BEATS (USING TWO CW LASERS)

Fig. 18

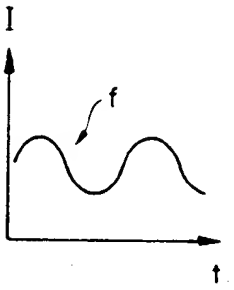
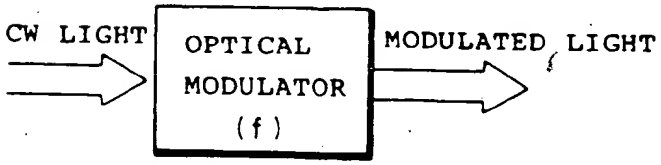
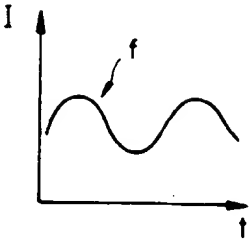


Fig. 19



METHOD FOR GENERATING MODULATED LIGHT WITH AN OPTICAL MODULATOR

Fig. 20



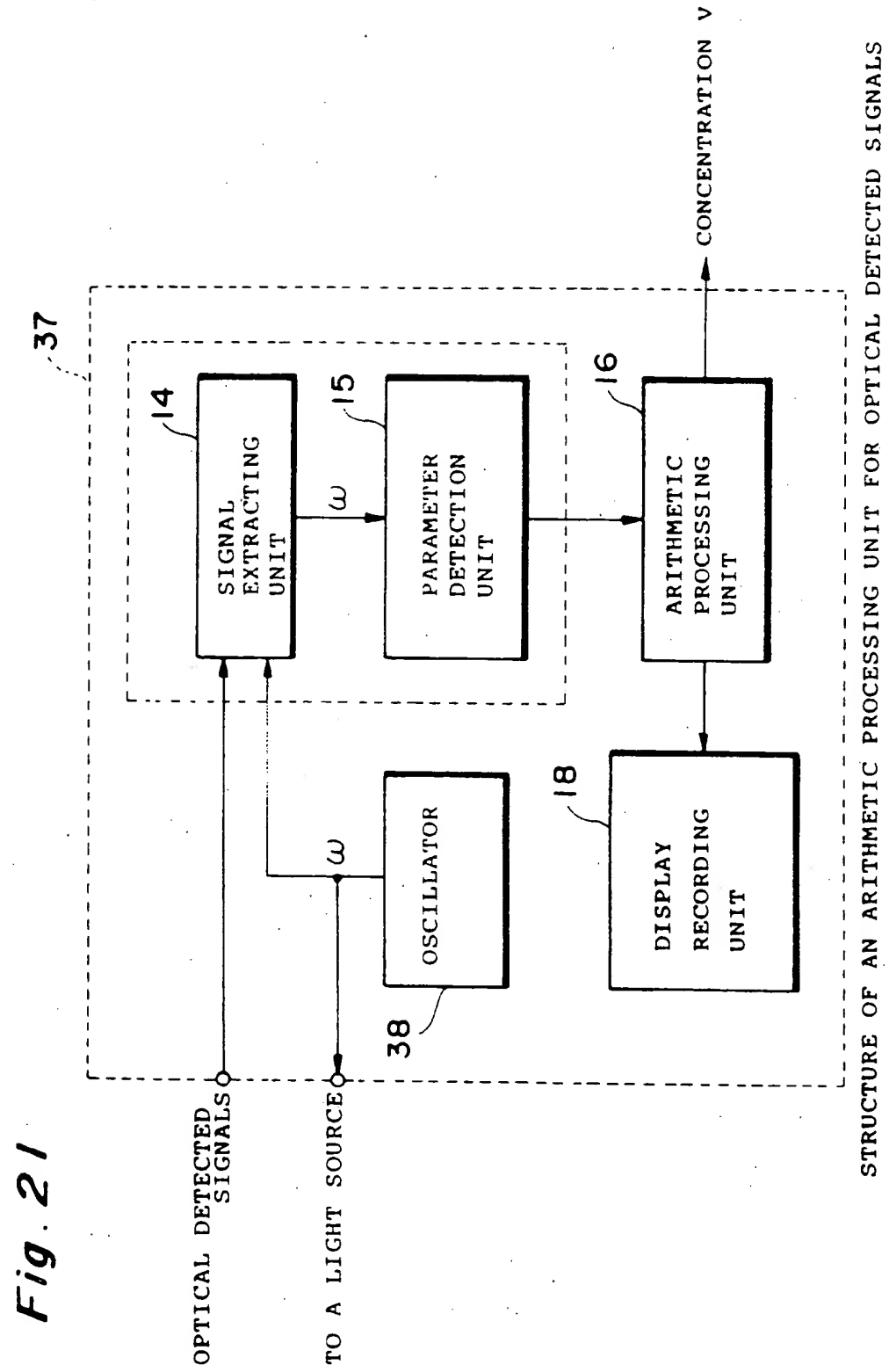

37
14
SIGNAL EXTRACTING UNIT
ω
15
PARAMETER DETECTION UNIT
16
ARITHMETIC PROCESSING UNIT
CONCENTRATION V
18
DISPLAY RECORDING UNIT
OSCILLATOR
38
ω
OPTICAL DETECTED SIGNALS
TO A LIGHT SOURCE
STRUCTURE OF AN ARITHMETIC PROCESSING UNIT FOR OPTICAL DETECTED SIGNALS

Fig. 21

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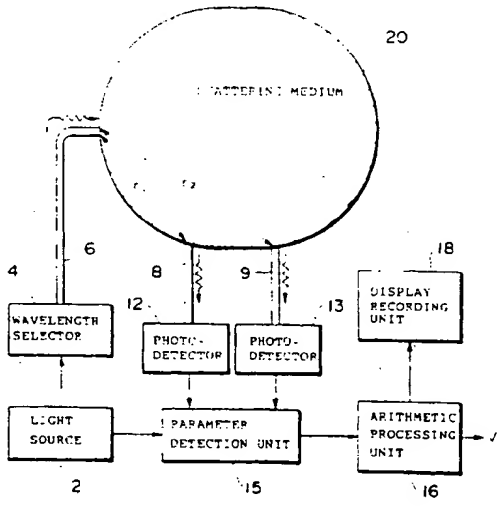
London SW1H 0RJ (GB)

(54) Method and apparatus for measuring concentration of absorptive constituent in scattering medium

(57) A method for measuring a concentration of an absorptive constituent in a scattering medium comprises the steps of emitting two or more kinds of light having predetermined wavelengths, making said light incident at a light incidence position into said scattering medium, detecting said light at one or more photodetection points to acquire one or more photodetection signals, detecting light quantities and average flight pathlengths for said respective kinds of light based on said signals, and obtaining a concentration of said absorptive constituent by arithmetic processing using said light quantities and average flight pathlengths based on a predetermined relationship. The method permits absolute-value measurement of the concentration of the absorptive constituent inside the scattering medium having various exterior shapes.

Fig. 4



STRUCTURE OF APPARATUS OF THE FIRST EMBODIMENT

EP 0 703 445 A3

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 95 30 6704

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	US 5 119 815 A (CHANCE BRITTON) 9 June 1992 * column 4, line 37 - column 5, line 43; figures 1-7 *	1,2,10, 11,19,20	G01N21/47 A61B5/00 G01N21/49
P,X	EP 0 628 804 A (HAMAMATSU PHOTONICS KK) 14 December 1994 * claims 1-3; figures 2,4 *	1,2,10, 11,19,20	
A	US 5 348 003 A (CARO RICHARD G) 20 September 1994 * column 5, line 5 - line 50 * * column 9, line 14 - column 10, line 13; claims 1,2 * * column 12, line 37 - column 13, line 58 *	1-4, 10-13	
A	WO 90 09003 A (NIM INC) 9 August 1990 * claims 1-4 *	1,3,4, 10,12,13	
A	WILSON B C ET AL: "OPTICAL REFLECTANCE AND TRANSMITTANCE OF TISSUES: PRINCIPLES AND APPLICATIONS" IEEE JOURNAL OF QUANTUM ELECTRONICS, vol. 26, no. 12, 1 December 1990, pages 2186-2199, XP000453579 * page 2193, right-hand column - page 2195, right-hand column *	1-4, 10-13	TECHNICAL FIELDS SEARCHED (Int.Cl.6) G01N A61B

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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	7 August 1997	Tabellion, M

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Application Number
EP 95 30 6704

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	FANTINI S ET AL: "QUANTITATIVE DETERMINATION OF THE ABSORPTION SPECTRA OF CHROMOPHORES IN STRONGLY SCATTERING MEDIA: A LIGHT-EMITTING-DIODE BASED TECHNIQUE" APPLIED OPTICS, vol. 33, no. 22, 1 August 1994, pages 5204-5213, XP000462186 * page 5205, left-hand column * * page 5206, right-hand column - page 5207, right-hand column * -----	1-4, 10-13	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)

The present search report has been drawn up for all claims

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